BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013292
Article Type:	Research
Date Submitted by the Author:	05-Jul-2016
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Primary Subject Heading:	Public health
Secondary Subject Heading:	Health economics
Keywords:	quality-adjusted life years, secondhand smoke, healthcare cost

Modeling lifetime costs and health outcomes attributable to secondhand smoke exposure at home among Korean adult women

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Running title: Simulation model analysis of SHS

Key words: secondhand smoking, husbands′ smoking, healthcare costs, QALYs, Korea

Word count:2,989

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ABSTRACT

Purpose: To estimate lifetime costs and health consequences for Korean adult women who were exposed to secondhand smoke (SHS) at home.

Methods: A Markov model was developed to project the lifetime healthcare costs and health outcomes of a hypothetical cohort of Korean women who are 40 years old and were married to current smokers. The Korean epidemiological data were used to reflect the natural history of SHS-exposed and non-exposed women. The direct healthcare costs (in 2014 US Dollars) and quality-adjusted life years (QALYs)) were annually discounted at 5% to reflect time preference. The time horizon of the analysis was lifetime and the cycle length was 1 year. Deterministic and probabilistic sensitivity analysis were conducted.

Results: The negative impact of SHS exposure was greater on QALYs (4.8%) than on life expectancy (3.1%). As discount rates increased or as the time horizon became shorter, the influence of SHS on health outcome was mitigated while the negative economic impact of SHS exposure (24.3%) escalated, suggesting that the adverse impact of SHS exposure on health outcomes may occur during the later part of the lifetime whereas direct healthcare costs attributable to SHS exposure may occur during the earlier part of the lifetime. The result was consistent across a wide range of assumptions.

Conclusion: Life expectancy might underestimate the impact of SHS exposure on health outcomes, especially if the time horizon of the analysis is not long enough. Early intervention on smoking behavior could substantially reduce direct healthcare costs attributable to SHS exposure.

STRENGTHS AND LIMICATIONS OF THIS STUDY

- Our study is the first attempt to project health and economic outcomes attributable to secondhand smoking (SHS) using a Markov simulation model.
- The model was validated by comparing its output against a population-based cohort study and the robustness of the assumptions were tested by conducting deterministic and probabilistic sensitivity analyses.
- Our results should be interpreted with caution, since they hinge on several assumptions due to insufficient and inconsistent data. Future research on the long-term impact of SHS should be followed.

INTRODUCTION

Nearly 6 million people are killed by tobacco annually, and more than 600,000 of these are non-smokers exposed to the secondhand smoke (SHS) or environmental tobacco smoke (ETS)[1,2]. Non-smokers in workplace or households are forced to be exposed to SHS, yet SHS in workplace is becoming less of an issue in many developed countries thanks to several smoke-free laws that have banned smoking in large buildings and restaurants[3,4]. However, few policies have been aggressive enough to ban smoking at home, leaving non-smokers in households exposed to SHS. Yet, measured nicotine and cotinine concentrations were significantly higher among SHS at home than among SHS at work, suggesting that SHS at home could cause significant health concerns[5,6]. SHS at home is of special concern in Korea, where the gender gap in smoking is especially high; only 4.3% of Korean adult women are smokers and 36.2% of Korean men are smokers as of 2013, whereas the Organization for Economic Cooperation and Development (OECD) reported that the average percentage of men and women smokers are 24.2% and 15.5%, respectively[1].

Several studies have reported that SHS exposure is associated with several health conditions, such as lung cancer, coronary heart disease, and respiratory disease in adults and sudden infant death syndrome in infants[7-9]. Increased morbidity and mortality result in increased healthcare costs among non-smokers exposed to SHS, which occurs over a lifetime. However, few studies have estimated the lifetime cost or expected health outcomes such as quality-adjusted life years (QALYs) attributable to SHS, much less in Asian countries where SHS exposure among women is especially high[1]. Most studies have calculated the annual cost of SHS[3,4,10], and several studies have estimated the cost attributable to smoking using a simulation model, yet they focused on the smokers, not the non-smokers exposed to SHS[11-14]. Several studies have conducted a cost-effectiveness analysis of smoking cessation drugs[15,16], yet those studies focused on the impact of smoking cessation drugs among smokers, and the SHS-exposed individuals were not considered in those studies.

The purpose of this study was to estimate health and economic outcomes of the lifetime cost of SHS at home among adult Korean women. More specifically, we sought to evaluate the direct healthcare cost and QALYs attributable to SHS among Korean adult women, who are highly vulnerable to the SHS exposure at home.

METHODS

Overview

A Markov model, the Secondhand smoking exposure outcome model (SHE model, Figure 1) was developed to project the economic and health outcomes associated with SHS at home among adult Korean females in their lifetime; more specifically, we compared the cost (in US dollars) and QALYs for the SHS exposed group with the SHS non-exposed group. The target population of the model was women aged 40 years old and who were married to current smokers, because the increased risk associated with SHS exposure was observed among middle-aged housewives[17,18].Our focus was on the direct medical costs attributable to SHS exposure; indirect or non-medical costs such as productivity costs and travel costs were not included in our analysis[19,20]. To capture the long-term impact of SHS exposure, the time horizon of the model was a lifetime[21] and the cycle length was set to one year, based on previous studies[14,15]. Due to data limitation, we focused on the SHS caused by current smokers, which made our projections rather conservative. TreeAge Pro 2015 Software (Williamstown, MA) was used to incorporate estimates from various literatures and build the mathematical simulation model. All future costs and outcomes were discounted to reflect people's positive time preference, namely, people prefer to receive benefits sooner than later, thus discounting adjusts the time preference by undervaluing future benefits to reflect the present value[20]. Both costs and health benefits were annually discounted at 5% based on economic evaluation guidelines [20,22], and publicly funded health care perspective was taken.

The Economic Model

A Markov state-transition simulation model was built to simulate the natural history of exposure to SHS[23] for the SHS exposed and SHS non-exposed groups based on epidemiological data. A defined set of health states and the transitions through them described the natural history of the disease (SHS exposure). Patients were assigned to a single health state at any given time, which was mutually exclusive and collectively exhaustive in terms of SHS disease characteristics[24].

To identify clinical conditions that influence the cost and health outcomes of the SHS exposed individuals at a statistically significant level, we reviewed previously published epidemiologic and cost studies and four conditions (lung cancer, myocardial infarction (MI), stroke, and asthma) were included in the SHE model[4,10,17,25-29]. Health conditions that were reported to trigger an elevated risk among SHS exposed women but whose influence was inconsistent or failed to reach a statistically significant level were not considered in our analysis[30,31].The model was progressive in nature; namely, once a patient developed a severe condition, such as lung cancer, the patients could not move into a milder condition such as asthma[16]. Thus, individuals in the event-free state can move to asthma, and patients in asthma cannot move back to the event-free state. Of those four conditions, three conditions (lung cancer, MI, and stroke) were further categorized as 1styear in event health state (such as stroke) and subsequent health states (such as post-stroke), because the cost of treating the health conditions and transition probabilities in the 1st year and following years differ significantly[32-34] (Figure 1).The model cycled annually until all individuals had moved to fatal states (died) or became 100 years old, at which point all of them were assumed to die[24].

Target population

We analyzed a cohort of 10,000 married non-smoking Korean women aged 40 years old at the time of the simulation and whose husband currently smoked 1 to 19 cigarettes daily because most studies on passive smoking focused on middle aged women, and those studies defined current smokers as such[17,18,25]. Our target population criterion is consistent with the habit of Korean male smokers because Korean male smokers consume 15.5 cigarettes per day on average[35]. We assumed that those women had been exposed to SHS at home since marriage, which translate into roughly 10 years of exposure.

Input data

Table 1 shows the input data used in the model with their respective references. Domestic cost and epidemiological data with large sample sizes were preferably sourced; foreign data were referenced when domestic data were not available. More specifically, the natural history of women non-exposed to SHS were estimated from domestic epidemiological studies[36-38] except for asthma, for which domestic data were not available[39], and the transition probabilities of the four conditions among SHS-exposed women were estimated using relative risk reported from published literature[17,25-28].

Relative Risk

To quantify the increased risk associated with the exposure to SHS, we referred to previous studies, focusing on meta-analyses or systematic reviews among passive smokers. Cohort or case-control studies with large sample sizes were also considered if few studies were available. A limited number of domestic studies were found, with Jee and colleagues' study on the effect of husbands' smoking on the incidence of lung cancer among 160, 130 Korean women aged 40~88 being the only domestic study identified by the authros[25]. Jee and colleagues reported that wives of current smokers were 2.0 times more likely to have lung cancer compared with their non SHS-exposed counterparts, and the increased risk was statistically significant at 0.05 level. Because Jee and colleagues' study definition of a current smoker (those who consume 1 to 19 cigarettes per day) is in line with the average number of daily cigarettes consumed by Korean male smokers, i.e. 15.5[35], we referred to the study. The increased risk of morbidity and mortality among the SHS-exposed group of other diseases (asthma, stroke, and MI) were estimated from non-Korean populations, due to data availability[17,26-28], and the increased risk associated with SHS exposure was assumed to be constant across the age group (Table 1).

Costs

Our study included direct medical costs attributable to SHS exposure. Costs of health states (first-year and subsequent year) were based on cost data estimated from the Korean National Health Insurance database[32,33,40]. The macro costing approach was employed[41], and direct non-medical costs, such as transportation costs, were not included in our analysis. Costs were adjusted by the medical care component of the Consumer Price Index in Korea[42], and then adjusted to 2014 US dollars[43].The annual direct costs in 2014 US dollars are summarized in Table 2.

QALY

To quantify the impact of SHS exposure on the health-related quality of life, we considered QALY, which incorporates life expectancy as well as the health-related quality of life[20]. The age- and sex- specific quality of life weights of the Korean general population were sourced from a national study that used EQ-5D[35], and the utility of SHS-exposed women who were event free was assumed to be the same as that of age-matched SHS-non-exposed women who were event free. The utilities corresponded to specific health states, as shown in Table 2,were obtained from a Korean catalogue of EQ-5D utility weights for chronic diseases[44]. For the utility of lung cancer, no domestic study was identified; thus, we referred to an Italian study that estimated the utility of lung cancer based on 95 patients using EQ-5D[45].

Sensitivity analysis

Because our projection was based on several assumptions, we conducted sensitivity analyses to investigate the robustness of the assumptions. For the univariate sensitivity analysis (where a single variable is varied over plausible ranges), we explored the impact of varied relative risk (95% confidence interval), discount rate (0, 3%, 7.5%), time horizon (5 years, 10 years, and 20 years), utilities (95% confidence interval), and annual cost (95% confidence interval) on the economic and health outcomes (Table 3). For the probabilistic sensitivity analyses, second-order Monte Carlo simulations were performed 10,000 times and visually presented in Figure 2. We employed a gamma distribution for cost, a lognormal distribution for relative risk, and a beta distribution for utilities[46].The results are visually presented as a scatterplot.

RESULTS

The SHE model predicted that in the absence of SHS exposure, Korean women will live 41.32 years and 34.56 QALYs before discount, which corresponded to 17.29 years and 15.35 QALYs after the 5% discount. The SHS-exposed women were predicted to live 37.91 years and 31.08 QALYs before discount and 16.76 years and 14.62 QALYs after the 5% discount (Table 3), suggesting that the negative impact of SHS exposure on the quality of life was greater than its impact on life expectancy regardless of the discount rate. The result also implied that SHS exposure was more associated with morbidity than mortality. Figure 2 illustrates that the life expectancy in the two groups was almost the same until they turned 75 years old, and the QALY curves from two groups diverged about 20 years earlier. As shown in Table 3, the negative influence of SHS on health outcomes was mitigated as the discount rate increased (from -8.3% to -1.7% for life expectancy and from -10.1% to -3.4% for QALYs) or time horizon became shorter (from -0.2% to -0.0% for life expectancy and from -1.9% to -0.5% for QALYs), suggesting that the adverse impact of SHS exposure on health outcomes was more likely to occur during the later part of the time horizon.

The estimated lifetime healthcare cost per women in the SHS non-exposed group was \$11,214 before the discount and \$2,465 after discount, whereas \$11,854 and \$3,065 for SHS exposed women before and after discount, respectively. The negative economic impact of SHS exposure escalated as the discount rates increased (from 5.7% to 33.8%), suggesting that the direct healthcare costs associated with SHS exposure were likely to occur during the earlier part of the time horizon. This result was consistent with the sensitivity analyses with different time horizons, where the negative economic impact of SHS exposure increased as the time horizon decreased (from 66.9% to 78%, Table 3, Figure 2 A).

The univariate sensitivity analysis showed that our results were robust across various assumptions except for the relative risk of lung cancer morbidity, which showed that SHS exposure had the highest negative economic impact (45.9% increase in direct healthcare expenditure) compared with non-exposed women. The probabilistic sensitivity analyses showed that SHS non-exposed women had similar health outcomes to the SHS-exposed women, but their expected healthcare costs varies more widely (Supplementary Figure 1); the healthcare costs and the QALYs for the non-exposed women varied from \$1,880 to \$3,131 (66.6% variation) and from 14.92 QALYs to 15.67 QALYs (5.0% variation), respectively. The variation was even higher for the SHS-exposed women, such that the healthcare costs and the QALYs varied from \$1,983 to \$4,303 (117.0% variation) and from 9.43 QALYs to 15.43 QALYs (63.5% variation), respectively.

Model Validation: effect of SHS exposure on lung cancer incidence

We estimated the impact of SHS exposure on health outcomes by incorporating the relative risk of specific diseases with various epidemiologic data. We compared our lung cancer incidence projections among SHS-exposed and non-exposed women with that reported by Jee et al[25]. Jee and colleagues reported 12.5 and 4.4 lung cancer per 100,000 person year for SHS- exposed and non-exposed women, respectively, which were similar to our study projections (10.12 and 5.16 lung cancer per 100,000 person year for SHS-exposed and non–exposed women, respectively).

DISCUSSION

The SHE model predicted that the SHS-exposed women incurred an additional $367 (before discount) or $600 (after discount) in their lifetime, and live 3.41 years (before discount) or 0.53 years (after discount) years shorter than their counterparts who were not exposed to SHS. Their QALYs are 3.48 QALYs (before discount) or 0.73 QALYs (after discount) lower than those of women not exposed to SHS. Several studies have estimated the economic impact of SHS exposure; Waters and colleagues analyzed the direct healthcare costs related with SHS exposure among Minnesota residents, and concluded that SHS exposure is associated with $44.58 per resident per year[47]. Max and colleagues reported that SHS was responsible for $241 million in healthcare cost and $119 million in lost productivity costs, resulting in $213 per non-smoker in California exposed to SHS[4]. Those studies reported a higher incremental cost compared with ours, which could be attributed to our conservative assumptions, such as excluding children and the loss of the productivity costs, only including health conditions with relative risks that are significantly increased, and assuming no utility difference between the SHS exposure status. Also, the healthcare cost in Korea is generally lower than that in the US thanks to Korea's National Health Insurance system. Thus, our healthcare cost estimate could actually underestimate the effect of the SHS exposure. Our estimate could refer to the lower bound of the healthcare costs associated with SHS exposure.

Our analysis suggested that the SHS-exposed women undergo higher health expenditures and lower QALYs/life expectancy, and the negative health effect of SHS exposure was greater on quality of life compared with that on life expectancy, regardless of various assumptions. In other words, SHS exposure was more closely associated with morbidity than mortality; thus, the SHS-exposed women might suffer more in terms of quality of life, compared with quantity of life. Our analysis indicated that the negative impact of SHS exposure on health outcome could be underestimated if life expectancy was solely used as a health outcome measure. Given the negative economic and health impact of SHS exposure at home, more aggressive smoking ban policies at home or more education for household members about the importance of SHS exposure should be considered.

Also, the SHE model illustrated that SHS exposure-attributable health costs were likely to occur earlier in their lifespan (e.g. their 50s) rather than later (e.g.in their 70s), implying that aggressive smoking bans or education on SHS at home as early as possible might be needed for those women who married current smokers, even though individuals in those age groups may not suffer from premature deaths.

Few studies have projected the impact of SHS exposure on quality of life. To our knowledge, our model is the first attempt to include QALYs in projecting health outcomes attributable to SHS exposure. Compared with previous studies, our Markov model has enhanced features because it has a lifetime horizon, incorporates QALYs, and allows subjects to move between specific health states[15].

The model-based approach has several strengths; it enables analysts to extrapolate beyond the observed time line and geographic settings, and synthesize data from multiple sources[21,24]. However, our results should be cautiously interpreted, since it hinges on several assumptions. First, the SHE model included 4 health conditions that demonstrated SHS exposure is associated with increased risk at a statistically significant level, but other conditions such as breast cancer, cervical cancer, and chronic obstructive pulmonary disease (COPD) have been shown to be associated with the SHS exposure, yet with conflicting results[25,30,31]. We excluded those conditions to reach more conservative conclusion, yet we could have underestimated the impact of SHS exposure.

Second, we only focused on SHS exposure, and thirdhand smoke (THS) exposure has been not considered in our analysis. THS exposure occurs when non-smokers are exposed to the residuals of nicotine or other chemicals on indoor surfaces caused by the tobacco smoke. Although THS exposure also could be associated with the negative impact of tobacco smoke, few studies have quantified the increased risk attributable to THS. Therefore, our study could not include the impact of THS.

Finally, although children and infants that reside with current smokers suffer from significant health burdens such as sudden infant death syndrome or various respiratory diseases[48,49], those populations were not included in our model. Given that children and infants are vulnerable to their parents' smoking behavior, further study is needed to estimate the impact of SHS on children and infants and to provide policy recommendations on these populations.

CONCLUSION

Although SHS exposure marginally decreased the life expectancy of exposed women, its negative impacts on quality of life and costs are substantial, and the result was consistent across a wide range of assumptions. Life expectancy might underestimate the impact of SHS exposure on health outcomes, especially if the time horizon of the analysis is not long enough. Early interventions for smoking behavior could especially reduce avoidable healthcare costs.

CONTRIBUTORSHIP STATEMENT

All authors participated in the design of the study. Ah Ram Han and JiyaeLee conducted systematic review of cost, utility, and epidemiology data. Jiyae Lee and SeungJin Bae built Markov simulation model and interpreted data. SeungJin Bae, Jiyae Lee and Kyung-Min Lim generated the manuscript, and Dalwoong Choi critically edited and commented on the manuscript. All authors read and approved the final manuscript.

FUNDING

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) and was funded by the Ministry of Education (2014R1A1A2058657).

COMPETING INTERESTS

None declared.

DATA SHARING STATEMENT

No additional data available

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Table 1. Annual incidence/mortality rate per disease states of Korean adult female population who are not exposed to SHS and the relative risk of morbidity and mortality related with SHS exposure used in the model.

Disease states	Age-specific incidence/mortality rate of Korean female					Relative Risk	
	40-49	50-59	60-69	70 and up	Reference	Point Estimate (95% CI)	References
Lung cancer							
Incidence[1]	0.01%	0.03%	0.07%	0.14%	[37]	2.00 (1.10-3.90)	[25]
Mortality[2]	21.09%	21.09%	21.09%	21.09%	[37]	1.31 (1.16–1.48)	[28]
Myocardial Infarction							
Incidence[1]	0.02%	0.09%	0.23%	0.54%	[36]	1.32 (1.04-1.67)	[17]
Mortality[3]	15.54%	12.19%	14.60%	28.92%	[36]	1.22 (1.14-1.30)	[17]
Stroke							
Incidence[1]	0.06%	0.20%	0.52%	1.47%	[36]	1.32 (1.14-1.53)	[27]
Mortality[4]	16.34%	8.23%	10.81%	27.00%	[36]	1.23 (1.07-1.40)	[27]
Asthma							
Incidence[1]	0.32%	0.32%	0.32%	0.32%	[39]	4.71 (1.29-16.80)	[26]
Mortality[5]	0.00%	0.00%	0.00%	0.03%	[38]		

1. Incidence rates among event-free individuals
2. Mortality rate among lung cancer patients
3. Mortality rates among myocardial infarction patients
4. Mortality rates among stroke patients
5. Mortality rates among asthma patients

Table 2. Annual SHS-related morbidity costs (in 2014 US dollar, $) and utility used in the model.

Disease states \ Age	Annual healthcare costs			Utility		
	1st year	Subsequent years	Reference	1st year	Subsequent years	Reference
Lung cancer	20,772	6,584	[32]	0.61	0.50	[45]
Myocardial Infarction	7,486	1,232	[33]	0.80		[44]
Stroke	7,735	1,003	[33]	0.58		[44]
Asthma	240		[40]	0.82		[44]

Table 3. Base-case and One-way sensitivity analyses for Korean adult female who are exposed to SHS at home compared with female not exposed.

Parameters	SHS exposure states	Direct health care costs (US dollar, $)		Life expectancy (Years)		Quality-Adjusted Life Years (QALYs)	
		Total	Incremental(%)	Total	Incremental(%)	Total	Incremental(%)
Base-case							
	No	2,465	-	17.29	-	15.35	-
	Yes	3,065	600(24.3%)	16.76	-0.53(-3.1%)	14.62	-0.73(-4.8%)
Discount rate							
0%	No	11,214	-	41.32	-	34.56	-
	Yes	11,854	640(5.7%)	37.91	-3.41(-8.3%)	31.08	-3.48(-10.1%)
3%	No	4,298	-	23.28	-	20.26	-
	Yes	5,012	714(16.6%)	22.20	-1.08(-4.6%)	18.96	-1.30(-6.4%)
7.5%	No	1,348	-	12.81	-	11.60	-
	Yes	1,804	456(33.8%)	12.59	-0.22(-1.7%)	11.20	-0.40(-3.4%)
Time horizon							
5 years	No	82	-	4.43	-	4.23	-
	Yes	146	64(78.0%)	4.43	-0.00(0.0%)	4.21	-0.02(-0.5%)
10 years	No	231	-	7.88	-	7.45	-
	Yes	417	186(80.5%)	7.87	-0.01(-0.1%)	7.37	-0.08(-1.1%)
20 years	No	706	-	12.62	-	11.71	-
	Yes	1,178	472(66.9%)	12.60	-0.02(-0.2%)	11.49	-0.22(-1.9%)
Relative risk of lung cancer morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,596	1,131(45.9%)	16.65	-0.64(-3.7%)	14.52	-0.83(-5.4%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,806	341(13.8%)	16.81	-0.48(-2.8%)	14.66	-0.69(-4.5%)
Relative risk of lung cancer mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,053	588(23.9%)	16.75	-0.54(-3.1%)	14.61	-0.74(-4.8%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,079	614(24.9%)	16.77	-0.52(-3.0%)	14.62	-0.73(-4.8%)

Relative risk of MI morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,194	729(29.6%)	16.75	-0.54(-3.1%)	14.60	-0.75(-4.9%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,966	501(20.3%)	16.77	-0.52(-3.0%)	14.63	-0.72(-4.7%)
Relative risk of CHD mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,059	594(24.1%)	16.76	-0.53(-3.1%)	14.61	-0.74(-4.8%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,071	606(24.6%)	16.77	-0.52(-3.0%)	14.62	-0.73(-4.8%)
Relative risk of stroke morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,243	778(31.6%)	16.75	-0.54(-3.1%)	14.58	-0.77(-5.0%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,913	448(18.2%)	16.77	-0.52(-3.0%)	14.65	-0.70(-4.6%)
Relative risk of CVD mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,047	582(23.6%)	16.74	-0.55(-3.2%)	14.60	-0.75(-4.9%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,083	618(25.1%)	16.79	-0.50(-2.9%)	14.63	-0.72(-4.7%)
Relative risk of asthma morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,869	404(16.4%)	16.27	-1.02(-5.9%)	13.66	-1.69(-11.0%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,255	790(32.0%)	17.05	-0.24(-1.4%)	15.08	-0.27(-1.8%)
Utilities of disease states							
Upper bound of 95% CI	No	-	-	-	-	15.62	-
	Yes	-	-	-	-	15.19	-0.43(-2.8%)
Lower bound of 95% CI	No	-	-	-	-	14.91	-
	Yes	-	-	-	-	13.45	-1.46(-9.8%)
Healthcare costs of disease states							
Upper bound of 95% CI	No	3,521	-	-	-	-	-
	Yes	4,378	857(24.3%)	-	-	-	-
Lower bound of 95% CI	No	1,595	-	-	-	-	-
	Yes	1,983	388(24.3%)	-	-	-	-

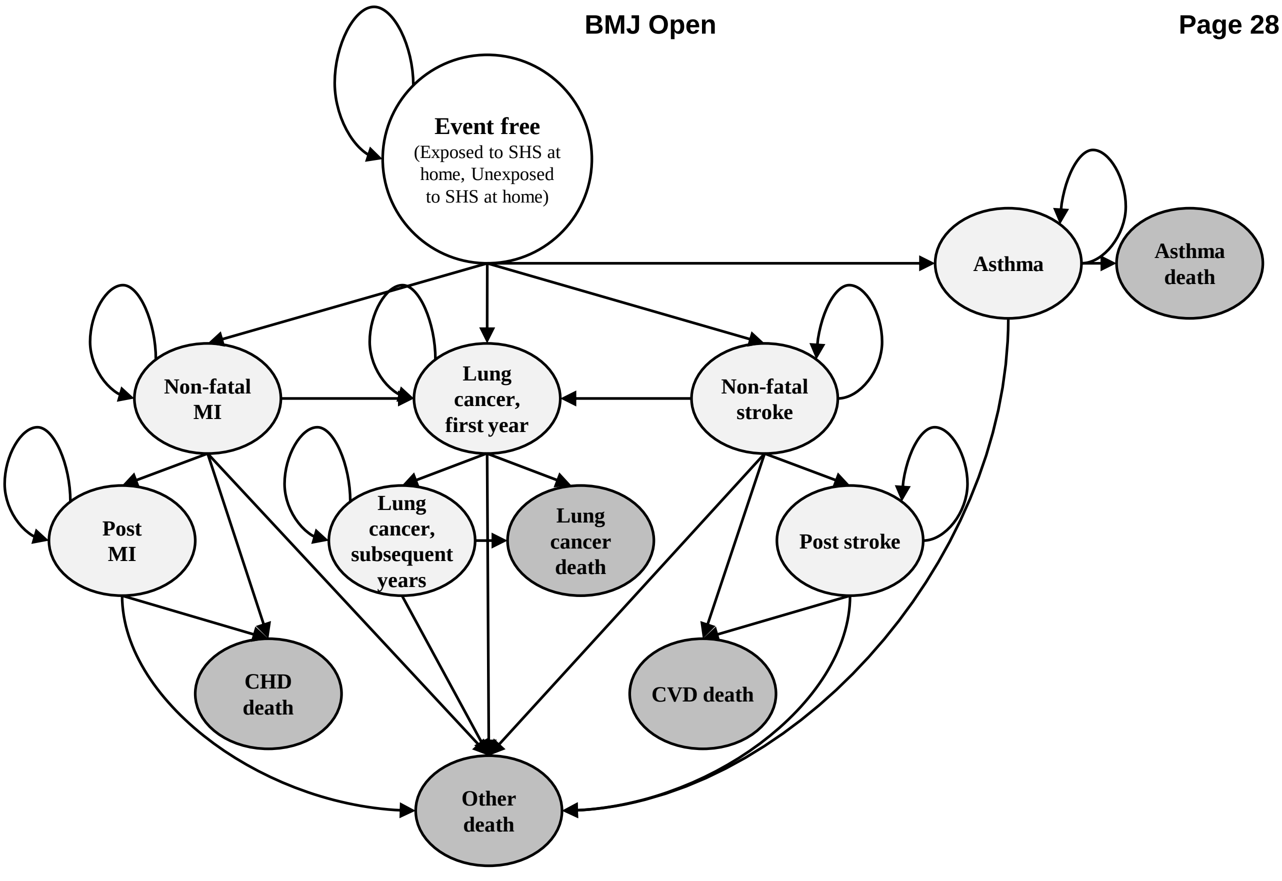


Figure 1 Transitions between disease states for Korean adult female who are exposed to secondhand smoke (SHS) at home. MI = myocardial infarction; CHD = coronary heart disease; CVD = cardiovascular disease

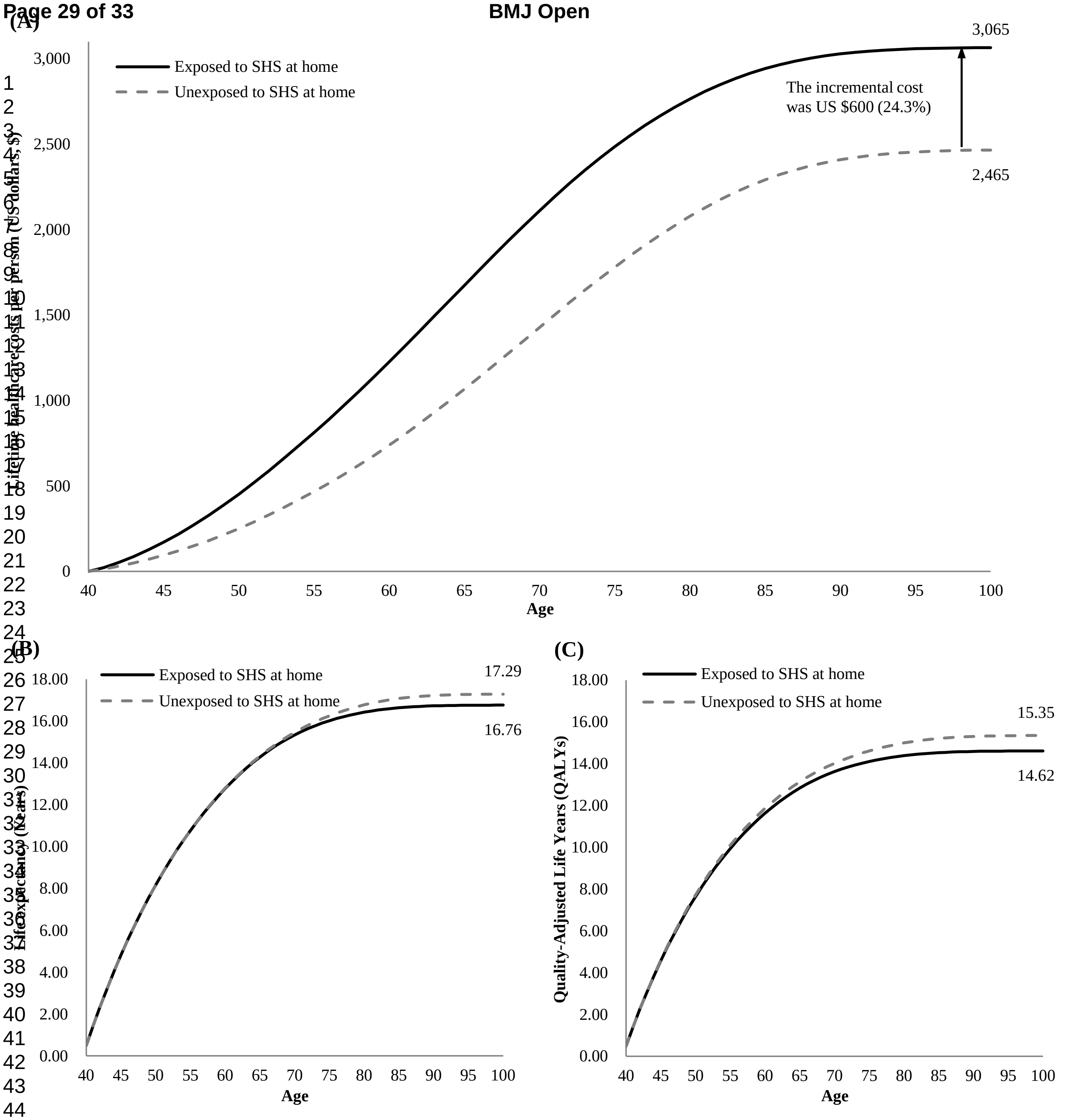
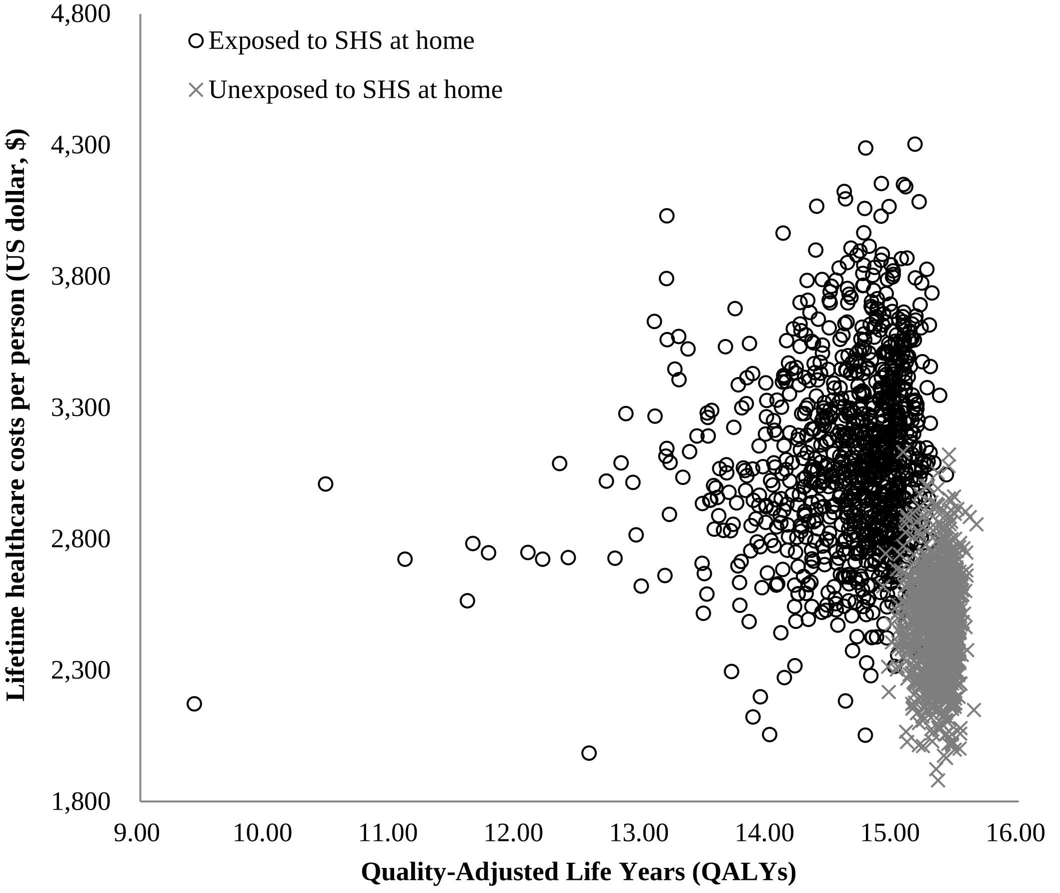


Figure 2 Cumulative lifetime healthcare costs, life expectancy, and quality-adjusted life years for Korean adult female who are exposed to secondhand smoke (SHS) at home compared with female not exposed (A) Lifetime healthcare costs (US dollars, $) (B) Life expectancy (Years) (C) Quality-Adjusted Life Years (QALYs)



Supplementary Figure 1. A scatter plot of second-order Monte Carlo simulations to calculate lifetime healthcare costs and quality-adjusted life years for Korean adult female who are exposed to secondhand smoke (SHS) at home in compared with female not exposed

	Unexposed			Exposed	
	Health care costs	QALYs		Health care costs	QALYs
Mean	2475.12	15.35	Mean	3107.03	14.64
Median	2473.50	15.37	Median	3081.71	14.78
Max	3130.67	15.67	Max	4303.30	15.43
Min	1879.67	14.92	Min	1983.21	9.43
difference	1250.99	0.74	difference	2320.09	5.99
%	66.6%	5.0%	%	117.0%	63.5%

EVEREST Statement: Checklist for health economics paper

	Study section	Additional remarks
Study design		
(1) The research question is stated	Introduction	Page 5
(2) The economic importance of the research question is stated	Introduction	Page 4-5
(3) The viewpoint(s) of the analysis are clearly stated and justified	Methods-Cost-effectiveness; Discussion	Publicly funded health care perspective (page 6)
(4) The rationale for choosing the alternative programmes or interventions compared is stated	Introduction	Yes (exposed vs. non-exposed, page 5)
(5) The alternatives being compared are clearly described	Background; Methods-Model construction	SHS-exposed vs. non SHS-exposed (page 5),
(6) The form of economic evaluation used is stated	Background; Methods-Cost-effectiveness (CE)	Since it is not a typical economic evaluation, it does not fall under traditional CE methodology
(7) The choice of form of economic evaluation is justified in relation to the questions addressed	Background; Discussion	Page 4
Data collection		
(8) The source(s) of effectiveness estimates used are stated	Methods-Assumptions used in the model; Table 1;	Table 1 & 2 (page 23,24)
(9) Details of the design and results of effectiveness study are given (if based on single study)	N/A	Data derived from national database, peer reviewed literature (page7-9)
(10) Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	Methods-Assumptions used in the model	Methods (sourced from previous studies; page 8)
(11) The primary outcome measure(s) for the economic evaluation are clearly stated	Methods-Model construction	Methods: Life expectancy, QALYS (page 5, 8)
(12) Methods to value health states and other benefits are stated	N/A	Methods (page 9)
(13) Details of the subjects from whom valuations were obtained are given	N/A	Sourced from peer-reviewed literature (Kang et al 2009, Value in Health, page 9
(14) Productivity changes (if included) are reported separately	N/A	Productivity costs not included in the

		analysis (page 5)
(15) The relevance of productivity changes to the study question is discussed	N/A	Discussion (page 12)
(16) Quantities of resources are reported separately from their unit costs	Methods-Cost calculations; Table 1	Table 1(utilization), Table 2 (unit cost)
(17) Methods for the estimation of quantities and unit costs are described	Methods-Cost calculations; Table 1	Unit costs were estimated based on Macro costing approach (page 8-9) utilization (quantity) was sourced from local data Page 8)
(18) Currency and price data are recorded	Methods-Cost calculations; Tables 1- 5	Methods (page 9)
(19) Details of currency of price adjustments for inflation or currency conversion are given	NA	Korean won was adjusted to US $ (page 9)
(20) Details of any model used are given	Methods-Model construction	Methods (page 5~10)
(21) The choice of model used and the key parameters on which it is based are justified	Methods-Model construction	Model structure (page 6), input data (page 7-9)
Analysis and interpretation of results		
(22) Time horizon of costs and benefits is stated	Methods-Model construction; Discussion	Methods (lifetime, page 5)
(23) The discount rate(s) is stated	N/A	5% (page 6)
(24) The choice of rate(s) is justified	N/A	Based on domestic PE recommendations (page 6)
(25) An explanation is given if costs or benefits are not discounted	N/A	N/A
(26) Details of statistical tests and confidence intervals are given for stochastic data	N/A	Page 9
(27) The approach to sensitivity analysis is given	Methods-Sensitivity analysis	Deterministic & stochastic sensitivity analysis were conducted (page 9-10)
(28) The choice of variables for sensitivity analysis is justified	Methods-Sensitivity analysis; Table 4	Methods (Page 9-10)
(29) The ranges over which the variables are varied are stated	Table 4	Table 3 (page 25-26)
(30) Relevant alternatives are compared	Methods-Model construction	Methods (page 5-6)

(31) Incremental analysis is reported	Methods-Cost-effectiveness; Table 2; Table 4	N/A
(32) Major outcomes are presented in a disaggregated as well as aggregated form	Table 2; Table 3	QALYs and life expectancy was reported separately (Table 3, page 25-26)
(33) The answer to the study question is given	Discussion; Conclusion	Discussion (page 12-13)
(34) Conclusions follow from the data reported	Conclusion	Page 14
(35) Conclusions are accompanied by the appropriate caveats	Discussion; Conclusion	Page 13-14

BMJ Open

Modeling lifetime costs and health outcomes attributable to secondhand smoke exposure at home among Korean adult women

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013292.R1
Article Type:	Research
Date Submitted by the Author:	14-Feb-2017
Complete List of Authors:	Lee, Jiyae; Ewha Womans University, College of Pharmacy Han, Ah Ram; Ewha Womans University, College of Pharmacy Choi, Dalwoong; Korea University, Department of Public Health Science Lim, Kyung-Min; Ewha Womans University, College of Pharmacy Bae, SeungJin; Ewha Womans University, College of Pharmacy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Health economics
Keywords:	quality-adjusted life years, secondhand smoke, healthcare cost

Modeling lifetime costs and health outcomes attributable to secondhand smoke exposure at home among Korean adult women

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Running title: Simulation model analysis of SHS

Key words: secondhand smoking, husbands′ smoking, healthcare costs, QALYs, Korea

Word count: 3,323

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ABSTRACT

Purpose: To estimate lifetime costs and health consequences for Korean adult women who were exposed to secondhand smoke (SHS) at home.

Methods: A Markov model was developed to project the lifetime healthcare costs and health outcomes of a hypothetical cohort of Korean women who are 40 years old and were married to current smokers. The Korean epidemiological data were used to reflect the natural history of SHS-exposed and non-exposed women. The direct healthcare costs (in 2014 US Dollars) and quality-adjusted life years (QALYs)) were annually discounted at 5% to reflect time preference. The time horizon of the analysis was lifetime and the cycle length was 1 year. Deterministic and probabilistic sensitivity analyses were conducted.

Results: In the absence of SHS exposure, Korean women will live 41.32 years or 34.56 QALYs before discount, which corresponded to 17.29 years or 15.35 QALYs after discount. The SHS-exposed women were predicted to live 37.91 years and 31.08 QALYs before discount and 16.76 years and 14.62 QALYs after discount. The estimated lifetime healthcare cost per women in the SHS non-exposed group was $11,214 before the discount and $2,465 after discount. The negative impact of SHS exposure on health outcomes and healthcare costs escalated as the time horizon increased, suggesting that the adverse impact of SHS exposure may have higher impact on the later part of the lifetime. The result was consistent across a wide range of assumptions.

Conclusion: Life expectancy might underestimate the impact of SHS exposure on health outcomes, especially if the time horizon of the analysis is not long enough. Early intervention on smoking behavior could substantially reduce direct healthcare costs and improve quality of life attributable to SHS exposure.

STRENGTHS AND LIMICATIONS OF THIS STUDY

- Our study is the first attempt to project health and economic outcomes attributable to secondhand smoking (SHS) using a Markov simulation model.
- The model was validated by comparing its output against a population-based cohort study and the robustness of the assumptions were tested by conducting deterministic and probabilistic sensitivity analyses.
- Our results should be interpreted with caution, since they hinge on several assumptions due to insufficient and inconsistent data. Future research on the long-term impact of SHS should be followed.

INTRODUCTION

Nearly 6 million people are killed by tobacco annually, and more than 600,000 of these are non-smokers exposed to the secondhand smoke (SHS) or environmental tobacco smoke (ETS)[1 2]. Non-smokers in workplace or households are forced to be exposed to SHS, yet SHS in workplace is becoming less of an issue in many developed countries thanks to several smoke-free laws that have banned smoking in large buildings and restaurants[3 4]. However, few policies have been aggressive enough to ban smoking at home, leaving non-smokers in households exposed to SHS. Yet, measured nicotine and cotinine concentrations were significantly higher among SHS at home than among SHS at work, suggesting that SHS at home could cause significant health concerns[5 6]. SHS at home is of special concern in Korea, where the gender gap in smoking is especially high; only 4.3% of Korean adult women are smokers and 36.2% of Korean men are smokers as of 2013, whereas the Organization for Economic Cooperation and Development (OECD) reported that the average percentage of men and women smokers are 24.2% and 15.5%, respectively[1].

Several studies have reported that SHS exposure is associated with several health conditions, such as lung cancer, coronary heart disease, and respiratory disease in adults and sudden infant death syndrome in infants[7-9]. Increased morbidity and mortality result in increased healthcare costs among non-smokers exposed to SHS, which occurs over a lifetime. However, few studies have estimated the lifetime cost or expected health outcomes such as quality-adjusted life years (QALYs) attributable to SHS, much less in Asian countries where SHS exposure among women is especially high[1]. Most studies have calculated the annual cost of SHS[3 4 10], and several studies have estimated the cost attributable to smoking using a simulation model, yet they focused on the smokers, not the non-smokers exposed to SHS[11-14]. Several studies have conducted a cost-effectiveness analysis of smoking cessation drugs[15 16], yet those studies focused on the impact of smoking cessation drugs among smokers, and the SHS-exposed individuals were not considered in those studies.

The purpose of this study was to estimate health and economic outcomes of the lifetime cost of SHS at home among adult Korean women. More specifically, we sought to evaluate the direct healthcare cost and QALYs attributable to SHS among Korean adult women, who are highly vulnerable to the SHS exposure at home.

METHODS

Overview

A Markov model, the Secondhand smoking exposure outcome model (SHE model, Figure 1) was developed to project the economic and health outcomes associated with SHS at home among adult Korean females in their lifetime; more specifically, we compared the cost (in US dollars) and QALYs for the SHS exposed group with the SHS non-exposed group. The target population of the model was women aged 40 years old and who were married to current smokers, because the increased risk associated with SHS exposure was observed among middle-aged housewives[17 18].Our focus was on the direct medical costs attributable to SHS exposure; indirect or non-medical costs such as productivity costs and travel costs were not included in our analysis[19 20]. To capture the long-term impact of SHS exposure, the time horizon of the model was a lifetime[21] and the cycle length was set to one year, based on previous studies[14 15]. Due to data limitation, we focused on the SHS caused by current smokers, which made our projections rather conservative. TreeAge Pro 2015 Software (Williamstown, MA) was used to incorporate estimates from various literatures and build the mathematical simulation model. All future costs and outcomes were discounted to reflect people's positive time preference, namely, people prefer to receive benefits sooner than later, thus discounting adjusts the time preference by undervaluing future benefits to reflect the present value[20]. Both costs and health benefits were annually discounted at 5% based on economic evaluation guidelines [20 22], and publicly funded health care perspective was taken.

The Economic Model

A Markov state-transition simulation model was built to simulate the natural history of exposure to SHS[23] for the SHS exposed and SHS non-exposed groups based on epidemiological data. A defined set of health states and the transitions through them described the natural history of the disease (SHS exposure). Patients were assigned to a single health state at any given time, which was mutually exclusive and collectively exhaustive in terms of SHS disease characteristics[24].

To identify clinical conditions that influence the cost and health outcomes of the SHS exposed individuals at a statistically significant level, we reviewed previously published epidemiologic and cost studies and four conditions (lung cancer, myocardial infarction (MI), stroke, and asthma) were included in the SHE model[4 10 17 25-29]. We considered 4 major health outcomes based on previous systematic reviews and official recommendations[9 26 28 30 31] and conditions whose causal association was inconclusive (such as breast cancer, COPD, cervical cancer)were not included[9 30].

Health conditions that were reported to trigger an elevated risk among SHS exposed women but whose influence was inconsistent or failed to reach a statistically significant level were not considered in our analysis[32 33].The model was progressive in nature; namely, once a patient developed a severe condition, such as lung cancer, the patients could not move into a milder condition such as asthma[16]. Thus, individuals in the event-free state can move to asthma, and patients in asthma cannot move back to the event-free state. Of those four conditions, three conditions (lung cancer, MI, and stroke) were further categorized as 1st year in event health state (such as stroke) and subsequent health states (such as post-stroke), because the cost of treating the health conditions and transition probabilities in the 1st year and following years differ significantly[34-36] (Figure 1).The model cycled annually until all individuals had moved to fatal states (died) or became 100 years old, at which point all of them were assumed to die[24].

Target population

We analyzed a cohort of 10,000 married non-smoking Korean women aged 40 years old at the time of the simulation and whose husband currently smoked 1 to 19 cigarettes daily because most studies on passive smoking focused on middle aged women, and those studies defined current smokers as such[17 18 25]. Our target population criterion is consistent with the habit of Korean male smokers because Korean male smokers consume 15.5 cigarettes per day on average[37]. We assumed that those women had been exposed to SHS at home since marriage, which translate into roughly 10 years of exposure.

Input data

Table 1 shows the input data used in the model with their respective references. Domestic cost and epidemiological data with large sample sizes were preferably sourced; foreign data were referenced when domestic data were not available. More specifically, the natural history of women non-exposed to SHS were estimated from domestic epidemiological studies[38-40] except for asthma, for which domestic data were not available[41], and the transition probabilities of the four conditions among SHS-exposed women were estimated using relative risk reported from published literature[17 25-28].

Relative Risk

To quantify the increased risk associated with the exposure to SHS, we referred to previous studies, focusing on meta-analyses or systematic reviews among passive smokers. Cohort or case-control studies with large sample sizes were also considered if few studies were available. A limited number of domestic studies were found, with Jee and colleagues' study on the effect of husbands' smoking on the incidence of lung cancer among 160,130 Korean women aged 40~88 being the only domestic study identified by the authors[25]. Jee and colleagues reported that wives of current smokers were 2.0 times more likely to have lung cancer compared with their non SHS-exposed counterparts, and the increased risk was statistically significant at 0.05 level. Because Jee and colleagues' study definition of a current smoker (those who consume 1 to 19 cigarettes per day) is in line with the average number of daily cigarettes consumed by Korean male smokers, i.e. 15.5[37], we referred to the study. The increased risk of morbidity and mortality among the SHS-exposed group of other diseases (asthma, stroke, and MI) were estimated from non-Korean populations, due to data availability[17 26-28], and the increased risk associated with SHS exposure was assumed to be constant across the age group (Table 1).

Costs

Our study included direct medical costs attributable to SHS exposure. Costs of health states (first-year and subsequent year) were based on cost data estimated from the Korean National Health Insurance database[34 35 42]. The macro costing approach was employed[43], and direct non-medical costs, such as transportation costs, were not included in our analysis. Costs were adjusted by the medical care component of the Consumer Price Index in Korea[44], and then adjusted to 2014 US dollars; 1 USD equals 1,053.22 Korean won as of 2014. [45].The annual direct costs in 2014 US dollars are summarized in Table 2.

QALY

To quantify the impact of SHS exposure on the health-related quality of life, we considered QALY, which incorporates life expectancy as well as the health-related quality of life[20]. The age- and sex- specific quality of life weights of the Korean general population were sourced from a national study that used EQ-5D[37], and the utility of SHS-exposed women who were event free was assumed to be the same as that of age-matched SHS-non-exposed women who were event free. The utilities corresponded to specific health states, as shown in Table 2,were obtained from a Korean catalogue of EQ-5D utility weights for chronic diseases[46]. For the utility of lung cancer, no domestic study was identified; thus, we referred to an Italian study that estimated the utility of lung cancer based on 95 patients using EQ-5D[47].

Sensitivity analysis

Because our projection was based on several assumptions, we conducted sensitivity analyses to investigate the robustness of the assumptions. For the univariate sensitivity analysis (where a single variable is varied over plausible ranges), we explored the impact of varied relative risk (95% confidence interval), discount rate (0, 3%, 7.5%), time horizon (5 years, 10 years, and 20 years), utilities (95% confidence interval), and annual cost (95% confidence interval) on the economic and health outcomes (Table 3). For the probabilistic sensitivity analyses, second-order Monte Carlo simulations were performed 10,000 times and visually presented in Supplementary Figure 1. We employed a gamma distribution for cost, a lognormal distribution for relative risk, and a beta distribution for utilities[48].The results are visually presented as a scatterplot.

RESULTS

The SHE model predicted that in the absence of SHS exposure, Korean women will live 41.32 years and 34.56 QALYs before discount, which corresponded to 17.29 years and 15.35 QALYs after the 5% discount. The SHS-exposed women were predicted to live 37.91 years and 31.08 QALYs before discount and 16.76 years and 14.62 QALYs after the 5% discount (Table 3), suggesting that the negative impact of SHS exposure on the quality of life was greater than its impact on life expectancy regardless of the discount rate. The result also implied that SHS exposure was more associated with morbidity than mortality. Figure 2 illustrates that the life expectancy in the two groups was almost the same until they turned 75 years old, and the QALY curves from two groups diverged about 20 years earlier. As shown in Table 3, the negative influence of SHS on health outcomes was mitigated as the discount rate increased (from -8.3% to -1.7% for life expectancy and from -10.1% to -3.4% for

QALYs) or time horizon became shorter (from -0.2% to -0.0% for life expectancy and from -1.9% to -0.5% for QALYs), suggesting that the adverse impact of SHS exposure on health outcomes was more likely to occur during the later part of the time horizon.

The estimated lifetime healthcare cost per women in the SHS non-exposed group was \$11,214 before the discount and \$2,465 after discount, whereas \$11,854 and \$3,065 for SHS exposed women before and after discount, respectively. The negative economic impact of SHS exposure escalated as the time horizon increased (from \$64 for 5 years to \$472 for 20 years, since the projected value for 20 years is more than 4 times of the values projected for 5 years, suggesting that the direct healthcare costs associated with SHS exposure have higher impact on the later part of the time horizon. This result was consistent with the sensitivity analyses with different discount rate, where the negative economic impact of SHS exposure increased as the time horizon increased (from 5.7% to 33.8%, Table 3, Figure 2 A).

The univariate sensitivity analysis showed that our results were robust across various assumptions except for the relative risk of lung cancer morbidity, which showed that SHS exposure had the highest negative economic impact (45.9% increase in direct healthcare expenditure) compared with non-exposed women. The probabilistic sensitivity analyses showed that SHS non-exposed women had similar health outcomes to the SHS-exposed women, but their expected healthcare costs varies more widely (Supplementary Figure 1); the healthcare costs and the QALYs for the non-exposed women varied from \$1,880 to \$3,131 (66.6% variation) and from 14.92 QALYs to 15.67 QALYs (5.0% variation), respectively. The variation was even higher for the SHS-exposed women, such that the healthcare costs and the QALYs varied from \$1,983 to \$4,303 (117.0% variation) and from 9.43 QALYs to 15.43 QALYs (63.5% variation), respectively.

Model Validation: effect of SHS exposure on lung cancer incidence

We estimated the impact of SHS exposure on health outcomes by incorporating the relative risk of specific diseases with various epidemiologic data. We compared our lung cancer incidence projections among SHS-exposed and non-exposed women with that reported by Jee et al[25]. Jee and colleagues reported 12.5 and 4.4 lung cancer per 100,000 person year for SHS- exposed and non-exposed women, respectively, which were similar to our study projections (10.12 and 5.16 lung cancer per 100,000 person year for SHS-exposed and non–exposed women, respectively).

DISCUSSION

The SHE model predicted that the SHS-exposed women incurred an additional $367 (before discount) or $600 (after discount) in their lifetime, and live 3.41 years (before discount) or 0.53 years (after discount) years shorter than their counterparts who were not exposed to SHS. Their QALYs are 3.48 QALYs (before discount) or 0.73 QALYs (after discount) lower than those of women not exposed to SHS. Several studies have estimated the economic impact of SHS exposure; Waters and colleagues analyzed the direct healthcare costs related with SHS exposure among Minnesota residents, and concluded that SHS exposure is associated with $44.58 (or $51.66 in 2014, adjusted by the medical care component of CPI) per resident per year[49]. Max and colleagues reported that SHS was responsible for $241 million in healthcare cost and $119 million in lost productivity costs, resulting in $213 per non-smoker in California exposed to SHS[4]. Those studies reported a higher incremental cost compared with ours, which could be attributed to our conservative assumptions, such as excluding children and the loss of the productivity costs, only including health conditions with relative risks that are significantly increased, and assuming no utility difference between the SHS exposure status. Also, the healthcare cost in Korea is generally lower than that in the US thanks to Korea's National Health Insurance system. Thus, our healthcare cost estimate could actually underestimate the effect of the SHS exposure. Our estimate could refer to the lower bound of the healthcare costs associated with SHS exposure. Based on Korean national survey in 2014, about 13.9% of female non-smoking adults are exposed to SHS at home[50]. It has been reported that about 13.9 million Korean females are aged 40 or older as of January 2016, thus about 1.9 million adult Korean females are estimated to be exposed to the SHS exposure at home, which translates into 1.16 Billion USD (13.9 million *incremental medical cost due to SHS exposure (600 incremental USD per person exposed to SHS) at national level.

Our analysis suggested that the SHS-exposed women undergo higher health expenditures and lower QALYs/life expectancy, and the negative health effect of SHS exposure was greater on quality of life compared with that on life expectancy, regardless of various assumptions. In other words, SHS exposure was more closely associated with morbidity than mortality; thus, the SHS-exposed women might suffer more in terms of quality of life, compared with quantity of life. Since the diseases caused by SHS exposure are likely to be of chronic nature but not of high mortality (such as asthma or MI), the exposed women are likely to chronically suffer from diseases caused by SHS exposure, thus their quality of life decreased, while their life expectancy is similar to that of the non-exposed. Thus, it is not surprising that we reached such conclusions.

Our analysis indicated that the negative impact of SHS exposure on health outcome could be underestimated if life expectancy was solely used as a health outcome measure. Given the negative economic and health impact of SHS exposure at home, more aggressive smoking ban policies at home or more education for household members about the importance of SHS exposure should be considered.

Also, the SHE model illustrated that SHS exposure-attributable health costs have higher impact on older adults (e.g. their 70s) who had been exposed to the SHS for longer period than earlier (e.g.in their 50s), implying that the impact of SHS exposure is aggravated for older age group, thus aggressive smoking bans or education on SHS at home as early as possible might be needed for those women who married current smokers, even though individuals in those age groups may not suffer from premature deaths.

Few studies have projected the impact of SHS exposure on quality of life. To our knowledge, our model is the first attempt to include QALYs in projecting health outcomes attributable to SHS exposure. Compared with previous studies, our Markov model has enhanced features because it has a lifetime horizon, incorporates QALYs, and allows subjects to move between specific health states[15].

The model-based approach has several strengths; it enables analysts to extrapolate beyond the observed time line and geographic settings, and synthesize data from multiple sources[21 24]. However, our results should be cautiously interpreted, since it hinges on several assumptions. First, the SHE model included 4 health conditions that demonstrated SHS exposure is associated with increased risk at a statistically significant level, but other conditions such as breast cancer, cervical cancer, and chronic obstructive pulmonary disease (COPD) have been shown to be associated with the SHS exposure, yet with conflicting results[25 32 33]. We excluded those conditions to reach more conservative conclusion, yet we could have underestimated the impact of SHS exposure.

Second, we only focused on SHS exposure, and thirdhand smoke (THS) exposure has been not considered in our analysis. THS exposure occurs when non-smokers are exposed to the residuals of nicotine or other chemicals on indoor surfaces caused by the tobacco smoke. Although THS exposure also could be associated with the negative impact of tobacco smoke, few studies have quantified the increased risk attributable to THS. Therefore, our study could not include the impact of THS.

In addition, our study was based on the current reported SHS exposure and did not consider SHS occurred in the past. Since most of the epidemiological studies we quoted considered spousal current smoking status and ignored whether those women had been exposed to the SHS in the past, which is a limitation.

Finally, although children and infants that reside with current smokers suffer from significant health burdens such as sudden infant death syndrome or various respiratory diseases[51 52], those populations were not included in our model. Given that children and infants are vulnerable to their parents' smoking behavior, further study is needed to estimate the impact of SHS on children and infants and to provide policy recommendations on these populations.

CONCLUSION

Although SHS exposure marginally decreased the life expectancy of exposed women, its negative impacts on quality of life and costs are substantial, and the result was consistent across a wide range of assumptions. Life expectancy might underestimate the impact of SHS exposure on health outcomes, especially if the time horizon of the analysis is not long enough. Early interventions for smoking behavior could especially reduce avoidable healthcare costs.

CONTRIBUTORSHIP STATEMENT

All authors participated in the design of the study. Ah Ram Han and JiyaeLee conducted systematic review of cost, utility, and epidemiology data. Jiyae Lee and SeungJin Bae built Markov simulation model and interpreted data. SeungJin Bae, Jiyae Lee and Kyung-Min Lim generated the manuscript, and Dalwoong Choi critically edited and commented on the manuscript. All authors read and approved the final manuscript.

FUNDING

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2014R1A1A2058657).

COMPETING INTERESTS

None declared.

DATA SHARING STATEMENT

No additional data available

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Table 1. Annual incidence/mortality rate per disease states of Korean adult female population who are not exposed to SHS and the relative risk of morbidity and mortality related with SHS exposure used in the model.

Disease states	Age-specific incidence/mortality rate of Korean female					Relative Risk	
	40-49	50-59	60-69	70 and up	Reference	Point Estimate (95% CI)	References
Lung cancer							
Incidence[1]	0.01%	0.03%	0.07%	0.14%	[37]	2.00 (1.10-3.90)	[25]
Mortality[2]	21.09%	21.09%	21.09%	21.09%	[37]	1.31 (1.16–1.48)	[28]
Myocardial Infarction							
Incidence[1]	0.02%	0.09%	0.23%	0.54%	[36]	1.32 (1.04-1.67)	[17]
Mortality[3]	15.54%	12.19%	14.60%	28.92%	[36]	1.22 (1.14-1.30)	[17]
Stroke							
Incidence[1]	0.06%	0.20%	0.52%	1.47%	[36]	1.32 (1.14-1.53)	[27]
Mortality[4]	16.34%	8.23%	10.81%	27.00%	[36]	1.23 (1.07-1.40)	[27]
Asthma							
Incidence[1]	0.32%	0.32%	0.32%	0.32%	[39]	4.71 (1.29-16.80)	[26]
Mortality[5]	0.00%	0.00%	0.00%	0.03%	[38]		

1. Incidence rates among event-free individuals
2. Mortality rate among lung cancer patients
3. Mortality rates among myocardial infarction patients
4. Mortality rates among stroke patients
5. Mortality rates among asthma patients

Table 2. Annual SHS-related morbidity costs (in 2014 US dollar, $) and utility used in the model.

Disease states \ Age	Annual healthcare costs			Utility		
	1st year	Subsequent years	Reference	1st year	Subsequent years	Reference
Lung cancer	20,772	6,584	[32]	0.61	0.50	[45]
Myocardial Infarction	7,486	1,232	[33]	0.80		[44]
Stroke	7,735	1,003	[33]	0.58		[44]
Asthma	240		[40]	0.82		[44]

Table 3. Base-case and One-way sensitivity analyses for Korean adult female who are exposed to SHS at home compared with female not exposed.

Parameters	SHS exposure states	Direct health care costs (US dollar, $)		Life expectancy (Years)		Quality-Adjusted Life Years (QALYs)	
		Total	Incremental(%)	Total	Incremental(%)	Total	Incremental(%)
Base-case							
	No	2,465	-	17.29	-	15.35	-
	Yes	3,065	600(24.3%)	16.76	-0.53(-3.1%)	14.62	-0.73(-4.8%)
Discount rate							
0%	No	11,214	-	41.32	-	34.56	-
	Yes	11,854	640(5.7%)	37.91	-3.41(-8.3%)	31.08	-3.48(-10.1%)
3%	No	4,298	-	23.28	-	20.26	-
	Yes	5,012	714(16.6%)	22.20	-1.08(-4.6%)	18.96	-1.30(-6.4%)
7.5%	No	1,348	-	12.81	-	11.60	-
	Yes	1,804	456(33.8%)	12.59	-0.22(-1.7%)	11.20	-0.40(-3.4%)
Time horizon							
5 years	No	82	-	4.43	-	4.23	-
	Yes	146	64(78.0%)	4.43	-0.00(0.0%)	4.21	-0.02(-0.5%)
10 years	No	231	-	7.88	-	7.45	-
	Yes	417	186(80.5%)	7.87	-0.01(-0.1%)	7.37	-0.08(-1.1%)
20 years	No	706	-	12.62	-	11.71	-
	Yes	1,178	472(66.9%)	12.60	-0.02(-0.2%)	11.49	-0.22(-1.9%)
Relative risk of lung cancer morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,596	1,131(45.9%)	16.65	-0.64(-3.7%)	14.52	-0.83(-5.4%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,806	341(13.8%)	16.81	-0.48(-2.8%)	14.66	-0.69(-4.5%)
Relative risk of lung cancer mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,053	588(23.9%)	16.75	-0.54(-3.1%)	14.61	-0.74(-4.8%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,079	614(24.9%)	16.77	-0.52(-3.0%)	14.62	-0.73(-4.8%)

Relative risk of MI morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,194	729(29.6%)	16.75	-0.54(-3.1%)	14.60	-0.75(-4.9%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,966	501(20.3%)	16.77	-0.52(-3.0%)	14.63	-0.72(-4.7%)
Relative risk of CHD mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,059	594(24.1%)	16.76	-0.53(-3.1%)	14.61	-0.74(-4.8%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,071	606(24.6%)	16.77	-0.52(-3.0%)	14.62	-0.73(-4.8%)
Relative risk of stroke morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,243	778(31.6%)	16.75	-0.54(-3.1%)	14.58	-0.77(-5.0%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,913	448(18.2%)	16.77	-0.52(-3.0%)	14.65	-0.70(-4.6%)
Relative risk of CVD mortality							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,047	582(23.6%)	16.74	-0.55(-3.2%)	14.60	-0.75(-4.9%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,083	618(25.1%)	16.79	-0.50(-2.9%)	14.63	-0.72(-4.7%)
Relative risk of asthma morbidity							
Upper bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	2,869	404(16.4%)	16.27	-1.02(-5.9%)	13.66	-1.69(-11.0%)
Lower bound of 95% CI	No	2,465	-	17.29	-	15.35	-
	Yes	3,255	790(32.0%)	17.05	-0.24(-1.4%)	15.08	-0.27(-1.8%)
Utilities of disease states							
Upper bound of 95% CI	No	-	-	-	-	15.62	-
	Yes	-	-	-	-	15.19	-0.43(-2.8%)
Lower bound of 95% CI	No	-	-	-	-	14.91	-
	Yes	-	-	-	-	13.45	-1.46(-9.8%)
Healthcare costs of disease states							
Upper bound of 95% CI	No	3,521	-	-	-	-	-
	Yes	4,378	857(24.3%)	-	-	-	-
Lower bound of 95% CI	No	1,595	-	-	-	-	-
	Yes	1,983	388(24.3%)	-	-	-	-

Figure 1. Health states and disease progression for Korean female adults who are exposed to secondhand smoke (SHS) at home.

MI = myocardial infarction; CHD = coronary heart disease; CVD = cardiovascular disease

Figure 2 Cumulative lifetime healthcare costs, life expectancy, and quality-adjusted life years for Korean adult female who are exposed to secondhand smoke (SHS) at home compared with female not exposed (A) Lifetime healthcare costs (US dollars, $) (B) Life expectancy (Years) (C) Quality-Adjusted Life Years (QALYs)

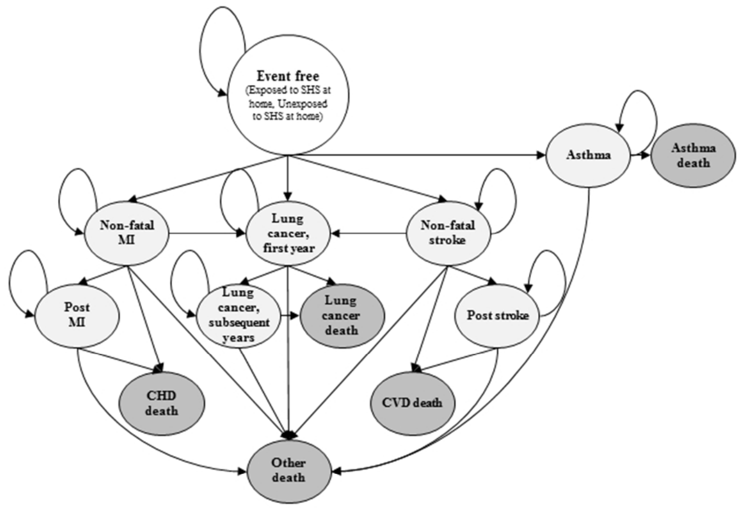

Figure 1. Health states and disease progression for Korean female adults who are exposed to secondhand smoke (SHS) at home.
MI = myocardial infarction; CHD = coronary heart disease; CVD = cardiovascular disease

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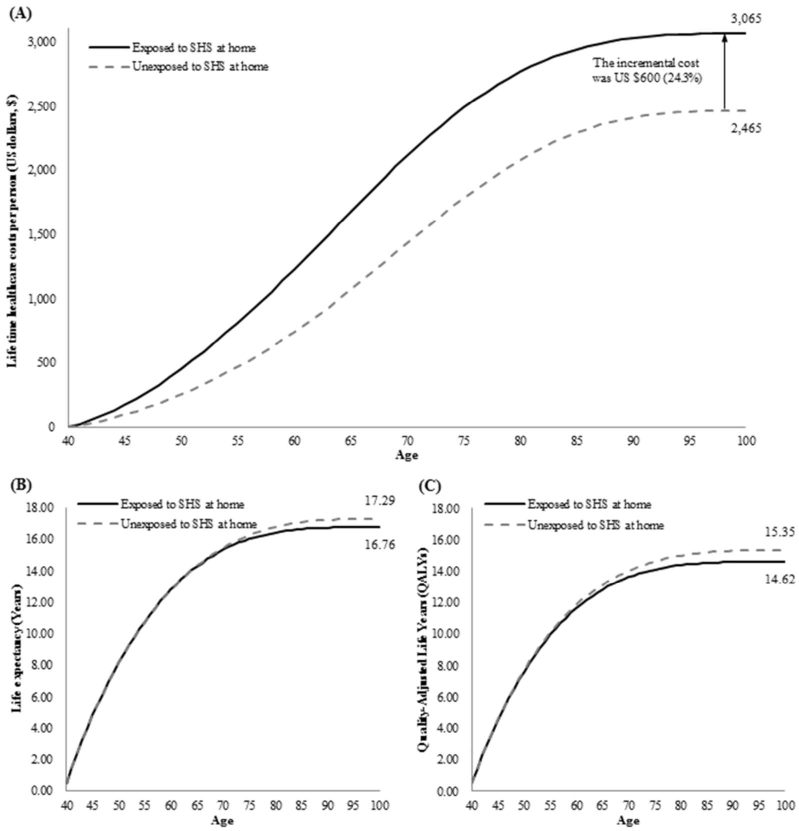

Figure 2 Cumulative lifetime healthcare costs, life expectancy, and quality-adjusted life years for Korean adult female who are exposed to secondhand smoke (SHS) at home compared with female not exposed (A) Lifetime healthcare costs (US dollars, $) (B) Life expectancy (Years) (C) Quality-Adjusted Life Years (QALYs)

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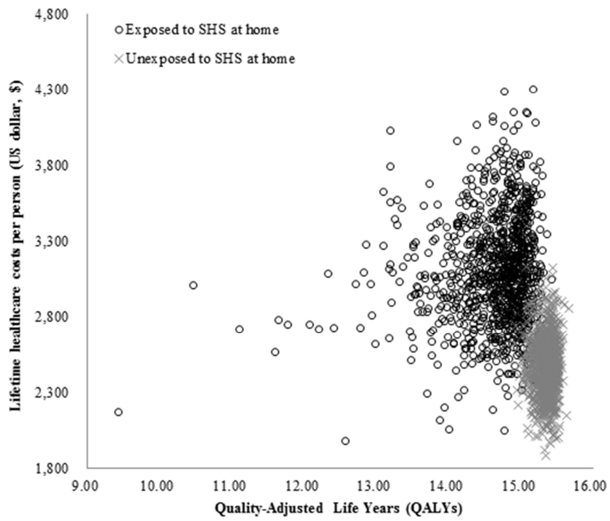

Supplementary Figure 1. A scatter plot of second-order Monte Carlo simulations to calculate lifetime healthcare costs and quality-adjusted life years for Korean adult female who are exposed to secondhand smoke (SHS) at home in compared with female not exposed

Unexposed			Exposed		
	Health care costs	QALYs		Health care costs	QALYs
Mean	2,475.12	15.35	Mean	3.107.03	14.64
Median	2,473.50	15.37	Median	3,081.71	14.78
Lower 5%	2,161.14	15.12	Lower 5%	2,553.42	13.60
Upper 5%	2,808.98	15.52	Upper 5%	3,735.65	15.18
Max	3,130.67	15.67	Max	4,303.30	15.43
Min	1,879.67	14.92	Min	1,983.21	9.43
Difference	1,250.99	0.74	difference	2,320.09	5.99
(Max vs.Min)%	66.6%	5.0%	(Max vs. Min) %	117.0%	63.5%

190x275mm (96 x 96 DPI)

EVEREST Statement: Checklist for health economics paper

	Study section	Additional remarks
Study design		
(1) The research question is stated	Introduction	Page 5
(2) The economic importance of the research question is stated	Introduction	Page 4-5
(3) The viewpoint(s) of the analysis are clearly stated and justified	Methods-Cost-effectiveness; Discussion	Publicly funded health care perspective (page 6)
(4) The rationale for choosing the alternative programmes or interventions compared is stated	Introduction	Yes (exposed vs. non-exposed, page 5)
(5) The alternatives being compared are clearly described	Background; Methods-Model construction	SHS-exposed vs. non SHS-exposed (page 5),
(6) The form of economic evaluation used is stated	Background; Methods-Cost-effectiveness (CE)	Since it is not a typical economic evaluation, it does not fall under traditional CE methodology
(7) The choice of form of economic evaluation is justified in relation to the questions addressed	Background; Discussion	Page 4
Data collection		
(8) The source(s) of effectiveness estimates used are stated	Methods-Assumptions used in the model; Table 1;	Table 1 & 2 (page 23,24)
(9) Details of the design and results of effectiveness study are given (if based on single study)	N/A	Data derived from national database, peer reviewed literature (page7-9)
(10) Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	Methods-Assumptions used in the model	Methods (sourced from previous studies; page 8)
(11) The primary outcome measure(s) for the economic evaluation are clearly stated	Methods-Model construction	Methods: Life expectancy, QALYS (page 5, 8)
(12) Methods to value health states and other benefits are stated	N/A	Methods (page 9)
(13) Details of the subjects from whom valuations were obtained are given	N/A	Sourced from peer-reviewed literature (Kang et al 2009, Value in Health, page 9
(14) Productivity changes (if included) are reported separately	N/A	Productivity costs not included in the

		analysis (page 5)
(15) The relevance of productivity changes to the study question is discussed	N/A	Discussion (page 12)
(16) Quantities of resources are reported separately from their unit costs	Methods-Cost calculations; Table 1	Table 1(utilization), Table 2 (unit cost)
(17) Methods for the estimation of quantities and unit costs are described	Methods-Cost calculations; Table 1	Unit costs were estimated based on Macro costing approach (page 8-9) utilization (quantity) was sourced from local data Page 8)
(18) Currency and price data are recorded	Methods-Cost calculations; Tables 1- 5	Methods (page 9)
(19) Details of currency of price adjustments for inflation or currency conversion are given	NA	Korean won was adjusted to US $ (page 9)
(20) Details of any model used are given	Methods-Model construction	Methods (page 5~10)
(21) The choice of model used and the key parameters on which it is based are justified	Methods-Model construction	Model structure (page 6), input data (page 7-9)
Analysis and interpretation of results		
(22) Time horizon of costs and benefits is stated	Methods-Model construction; Discussion	Methods (lifetime, page 5)
(23) The discount rate(s) is stated	N/A	5% (page 6)
(24) The choice of rate(s) is justified	N/A	Based on domestic PE recommendations (page 6)
(25) An explanation is given if costs or benefits are not discounted	N/A	N/A
(26) Details of statistical tests and confidence intervals are given for stochastic data	N/A	Page 9
(27) The approach to sensitivity analysis is given	Methods-Sensitivity analysis	Deterministic & stochastic sensitivity analysis were conducted (page 9-10)
(28) The choice of variables for sensitivity analysis is justified	Methods-Sensitivity analysis; Table 4	Methods (Page 9-10)
(29) The ranges over which the variables are varied are stated	Table 4	Table 3 (page 25-26)
(30) Relevant alternatives are compared	Methods-Model construction	Methods (page 5-6)

(31) Incremental analysis is reported	Methods-Cost-effectiveness; Table 2; Table 4	N/A
(32) Major outcomes are presented in a disaggregated as well as aggregated form	Table 2; Table 3	QALYs and life expectancy was reported separately (Table 3, page 25-26)
(33) The answer to the study question is given	Discussion; Conclusion	Discussion (page 12-13)
(34) Conclusions follow from the data reported	Conclusion	Page 14
(35) Conclusions are accompanied by the appropriate caveats	Discussion; Conclusion	Page 13-14